interfere with the care of a patient who is sick or injured. In these circumstances, who is to make the judgment of what is to be done? The patient, the physician, and various third parties each has much at stake. Retrospective judgments are likely to be arbitrary and usually unfair to someone. Prospective judgments may be equally arbitrary and unfair, and themselves costly and time consuming if everyone is consulted who might be. It would appear that the best and most economic medical care rests upon the good judgment of those involved at the time and place the care is given. It therefore follows that if improvements are to be made the emphasis should be upon improving judgment, and not upon punishment or professional liability or close governmental regulation of individual circumstances which by their nature defy standardization. It would appear then that the primary focus should be upon peer review of what actually takes place and upon the continuing education of all concerned. It may be necessary to take steps to ensure that all who are properly concerned, and not just physicians, become more involved in both these processes. Peer review and continuing education have been and continue to be among the primary goals of the California Medical Association. The CMA is an acknowledged leader in both these activities, which must now be further developed and expanded until they are acknowledged to meet the need. Absent a fair, effective, comprehensive peer review system, someone will fill the void, and it does not take much imagination to guess who it will be.

—MSMW

Mycoplasmas

MYCOPLASMAS ARE THE smallest living things able to grow outside of cells. Elsewhere in this issue of CALIFORNIA MEDICINE, Harwick, Kalmanson and Guze have reviewed the pathogenic potentialities of these organisms for man. In this respect some mycoplasmas occupy a position analogous to the staphylococcus in that many people are carriers but few become infected while Mycoplasma pneumoniae is more analogous in pathogenicity to the pneumococcus or Streptococcus hemolyticus. Each species of virulent mycoplasma has strict tissue tropism and host specificity and in this they more closely resemble viruses. Because several saprophytic mycoplasmas are commonly found in man, diagnostic significance of an isolate is not established until the organism is identified by serology or other suitable tests.

The incidence of penumonia caused by Mycoplasma pneumoniae has now been estimated in several parts of the world. The disease tends to occur in sporadic outbreaks without seasonal pattern. At the peak of such outbreaks the prevalence seldom equals or exceeds that of an epidemic of influenza type A or B. As with the viral respiratory infections, M. pneumoniae is responsible for a considerable amount of febrile illness, without pneumonia, which closely resembles the milder forms of influenza.

Apparently M. pneumoniae spreads less readily than influenza virus but crowded living conditions can greatly increase the rate of infection. As pointed out by Harwick, Kalmanson and Guze in their current review, atypical pneumonia was an important problem during World War II and sometimes still is in Army training centers. In the civilian population, outbreaks confined to a school or a family are common. A formalin-killed M. pneumoniae vaccine is available but its effectiveness is marginal and there is some doubt as to whether it is necessary for the civilian population in general. Mortality from M. pneumoniae infection is now very low. However, given a return of the conditions seen in 1940-45, the need for an effective vaccine might become urgent.

When grown on artificial medium for a hundred or more serial passages, M. pneumoniae becomes attenuated for man and experimental animals. But such attenuated strains when sprayed into the respiratory tract of volunteers still cause illness in some individuals. Chanock and his associates have developed temperature sensitive mutants of M. pneumoniae which, in experimental animals, infect the respiratory tract but grow

less readily at 37°C than at 32°C and seldom produce pneumonia.[1] Temperature-sensitive mutants of viruses such as influenza and respiratory syncytial have also been obtained for possible use in vaccination by the respiratory route. Current concepts point to this route of immunization for control of respiratory disease because some local stimulation of lymphocyte mediated immunity may occur and production of IgA secretory antibodies is said to be favored. The safety factor remains to be investigated more thoroughly. Also under investigation is the possibility of using antigens isolated from M. pneumoniae for immunization as has been done with the specific polysaccharide antigens of pneumococci.

The use of relatively ineffective formalized vaccines is not free of hazards. Not unlike the experience with inactivated measles vaccine was the finding of at least one group of investigators that the incidence and severity of illness among those without detectable antibodies following M. pneumoniae vaccine was greater than in the controls.[2] A possible explanation for this paradox is that no antibodies were present on the surface of the respiratory epithelium to prevent infection. When infection did occur, the resulting inflammatory reaction caused the exudation of antibody produced in a secondary response over the cells already infected and immunological damage resulted from the interaction with mycoplasmas closely associated with cell membranes.

Various relatively rare complications of M. pneumoniae infection have been mentioned in the review and in numerous other publications, but it is not clear whether they are due to direct infection or to autoimmune reactions. The hemolytic anemias associated with high titers of cold agglutinins seem clearly due to antibodies against the patient's own erythrocytes. Actually the cold agglutinins are only one aspect of a heterophile response in this disease. Complement fixing antibodies most reactive at 4°C with extracts of normal tissue are found frequently in late serum specimens. If such antibodies reach a very high titer it is conceivable that they might, by analogy to cold agglutinins, produce complement mediated tissue damage, for example in the nervous system.

Mycoplasmas found in the genitourinary tract are spread principally by the venereal route. In contrast to the high rate of positive cultures in adults for T strains and M. hominis, these organisms are found much less frequently in children and among groups of adults with restricted sexual activity. In its pathogenicity M. hominis resembles some types of infection with pyogenic cocci. Knowledge about disease produced by T strains is recent and still emerging. Antibody titers are generally low in the presence of positive cultures for these organisms, which indicates a carrier state rather than active infection, but in a few cases rising titers or high titers have been demonstrated. Isolation of a T strain in pure culture from the chorion, amnion, and decidua of a fetus with well defined pathologic change suggests occasional intrauterine infection.[3] A color reaction dependent on the production of ammonia from urea has been developed for the identification of T strain colonies on agar.[4] Of some importance with respect to use of antibiotics is the observation that lincomycin is significantly more inhibitory *in vitro* for M. hominis than for T strains. The latter, but not M. hominis, are very sensitive to erythromycin.[5]

The excitement, several years ago, about the association of mycoplasmas with leukemia has subsided after several different strains isolated from blood or bone marrow were identified as supposed saprophytes or animal pathogens. Since viruses and bacteria can also be similarly isolated at the later stages of the disease, it seems likely that deficiencies in the defense mechanism may account for the results. In my laboratory, cultures in the early stages of leukemia from bone marrow to media or tissue culture gave completely negative results (D. P. Sinha, unpublished). It is of interest, however, that some mycoplasmas show a definite tropism for leukemic cells *in vitro*. With other tissue cultures the significance of alterations in the chromosome pattern by persistent mycoplasmal infection needs further evaluation.

In animals the tropism of some well defined pathogenic mycoplasmas for serosa and endothelium is of interest in relation to similarities between the diseases they cause and human diseases of unknown cause. Mycoplasmas cause arthritis in cattle, goats, mice and birds. In these and other species mycoplasmal infection is associated with peritonitis, pericarditis, endocarditis and chronic vascular lesions. The perfect medium for isolation of human mycoplasmas has

not yet been discovered. It should be remembered that, for a number of years, T strains and M. pneumoniae could be grown only in chick embryos until suitable artificial media were devised. Attempts to grow mycoplasmas from human sources in tissue culture are hampered by the frequent contamination of such cultures with non-cytopathic strains. Controls carried without any inoculation are necessary. In choosing tissues to be grown *in vitro* for isolation of mycoplasmas, the probability of success would be greatly enhanced by attention to tropism and host specificity. The optimum would be human embryonic tissue from the same part of the body as that affected in a suspected mycoplasmal disease.

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A Trial Balloon

THERE IS MUCH TO SUGGEST that the Orwellian age is upon us and that it is arriving more or less on schedule. Take research and development in medicine and the health sciences for example. Medical schools are rapidly becoming dependent upon federal funding for the major part of both their research and educational functions, and federal guidelines and incentives are increasingly indicating the areas where research is to be done and how and for what students are to be trained. What is to be done is being decided not by educators, or by the professions or even by the public who pays the bills, but by planners in the federal bureaucracy and the politicians who listen to them, who together have control of the essential funds which are now the lifeblood of research and education in the health sciences. Unfortunately the record to date is that they have not been all that omniscient about it. And worse, all the conditions are now present which are necessary to assure conformity, mediocrity and, yes, in a very real sense thought control in research and development (including education) in health care, as federal funds are increasingly distributed through federally controlled channels for federally controlled purposes.

An alternative has been suggested by Jack H. Hall, M.D., to the Association for Hospital Medical Education. He suggests that the health industry should provide for its own research and development (including its own professional education) largely from its own funds. If ten percent of a $70 billion a year industry were so allocated (which seems about par), $7 billion would be available annually for medical research, professional education and experimentation in the delivery of health care. He suggests that this money be collected by some sort of use tax upon every aspect of the industry. A percentage would be retained by the originating group, institution or agency for its own research and development purposes, a percentage retained for use at the community, region or state level at their discretion, and a percentage made available for allocation to meet identified needs at the national level. The allocations and expenditures at the various levels would be decided upon with appropriate involvement of all who should be involved in both the public and private sectors, and not always determined by what someone who may or may not know, decides is best for us all. The sums available would have the advantage of being relatively constant and assured, and not so subject to the changing whims of planners and politicians as is so often now the case. And above all, those who are directly involved, and therefore more likely to have direct knowledge of what the real world problems are, and which ones are capable of solution, could have more to say about the allocation of funds for research, education and development for the health care industry.